REMARKS

Status of the Claims

Claims 1-3, 11, 14, 17, 20-26, 37, 38, 43, 65, 66, 68, 95, 120, 121, 123, 126, 167-171, 173, 175, 178 and 199-203 are in the application.

Claims 1-3, 11, 14, 17, 20-26, 37, 38, 43, 65, 66, 68, 95, 120, 121, 123, 126, 167-171, 173, 175, 178 and 199-203 were rejected.

By way of this amendment, claim 1 is amended; claims 2, 3, 11, 14, 17, 20-26, 37, 38, 43, 65, 66, 68, 95, 120, 121, 123, 126, 167-171, 173, 175, 178, 199-203 are herein cancelled without prejudice or concession, and new claims 204-223 are added.

Upon entry of this amendment, claims 1 and 204-223 will be pending.

Summary of the Amendment

Support for new claim 1 is to be found *inter alia* in the corresponding original claim 1 and in the description as filed at page 7, lines 26-28, and at page 28 lines 22-27.

Support of new claim 204 is to be found *inter alia* in original claim 17.

Support of new claim 205 is to be found *inter alia* in original claim 26.

Support of new claim 206 is to be found *inter alia* in original claim 28 and in the description as filed at page 22, lines 22-24.

Support of new claims 207 to 210 is to be found *inter alia* in original claims 29 to 33.

Support of new claims 211 to 213 is to be found *inter alia* in original claims 167 and 169.

Support of new claims 214 to 216 is to be found *inter alia* in original claims 170, 171 and 173.

Support of new claims 217 and 218 is to be found *inter alia* in original claims 10 and 11.

Support of new claim 219 is to be found *inter alia* in the description as filed at page 21, line 10.

Support of new claim 220 is to be found *inter alia* in original claim 12.

Support for new claim 221 is to be found *inter alia* in original claim 14.

Support for new claims 222 and 223 is to be found *inter alia* in original claims 37 and 38.

Accordingly, no new matter is added by these amendments, and entry is requested.

Claim Rejections – 35 USC § 102

In the Office Action mailed March 25, 2010 under items 2-10, the examiner has alleged that the claims lack novelty over US Pat. No. 6,245,331 ('331); US Pat. No. 5,116,766 ('766); US Pat. No. 5,932,705 ('705); US Pat. No. 6,416,962 ('962); WO 1999/00671 ('671); US Pat. No. 5,670,312 ('312); Ranadive *et al*., (1986) Clin Exp Immuno. 64:277-284 (Ranadive *et al*); Romain *et al*., (1993) Infec. Immun. 61(2):742-750 (Romain *et al*); and Kronberg *et al*., (1992) APMIS 100: 175-182 (Kronberg *et al*), cited in International Search Report (ISR) issued in respect of PCT/AU2004/000856.

Specifically, the examiner alleges that the subject matter of claims 1 to 3, 11, 14, 17, 20 to 26, 37, 38, 43, 65, 66, 68, 95, 120, 121, 123, 126, 167 to 171, 173, 175, 178, 199 to 203 has been previously disclosed by '331, '766, '705, '962, '671, '312, Ranadive *et al*, Romain *et al* and/or Kronberg *et al*.

Claims 2-3, 11, 14, 17, 20, 21, 26, 37, 38, 167-171 and 199-203 have been cancelled without prejudice or concession, thereby rendering these allegations moot in respect of those claims.

Claim 1 has been amended to define a method for identification of an immunogenic protein or fragment thereof capable of eliciting an immune response by providing a protein complex comprising an immunoglobulin having bound thereto an immunogenic protein of protein fragment by antigen-antibody interactions, wherein the protein complex has been previously obtained from a subject that has elicited an immune response against said immunogenic protein or fragment thereof, and identifying the protein fragment which is bound to the immunoglobulin. Accordingly, the claimed invention clearly requires obtaining from a subject an endogenous protein complex (i.e. a protein complex formed and present in the subject, not formed *ex vivo*) comprising "an immunoglobulin and a protein or fragment thereof bound to said immunoglobulin by virtue of an antigen-antibody interaction" and identifying an immunogenic protein or fragment thereof which is bound to the immunoglobulin in the complex by virtue of an antigen-antibody interaction i.e., in the subject.

'331, '705, '962, '671, '312, Ranadive et al and/or Romain et al

Amended claim 1 and claims 204 to 223 are novel over each one of '331, '705, '962, '671, '312, Ranadive *et al* and/or Romain *et al* by virtue *inter alia* of the step of providing a sample comprising immunoglobulin having bound thereto the immunogenic protein or protein fragment, and identifying the immunogenic protein or fragment in the protein complex. In fact all claims require an immunogenic protein or fragment to be bound to immunoglobulin in a sample derived previously from a subject.

Before the applicant's priority date, a step of identifying proteins bound to an immunoglobulin obtained as a protein complex in the sample from a subject was counter-intuitive, since according to conventional wisdom in the art, proteins were known to be rapidly degraded during infection (see page 6, lines 3 to 10 of the subject specification as filed). The claimed result is also surprising since conventional wisdom in the art at the priority date would

predict that antigen processing yields protein fragments that would be too small to be recognized by amino acids sequence analysis.

With respect to '331 and '705, we respectfully submit that '331 and '705 merely suggest immunoprofiling methods, whereby proteins from bacterium are separated by electrophoresis and then probed with serum from a subject infected with that bacterium to identify proteins against which a subject has raised antibodies. Accordingly, '331 and '705 specifically require an *ex vivo* step of contacting proteins from a bacterium with a sample. Accordingly we submit that all claims are novel over '331 and '705.

Similarly, '312 merely suggests immunoprofiling method whereby antibodies from patient sera are isolated and immobilized on solid support surface and a library of peptides displayed on the surface of bacteriophage is brought into contact with the immobilized antibodies, to thereby identify disease specific antibodies raised by the subject (see e.g., column 3, lines 15-63). Accordingly, '312 also requires an *ex-vivo* step of contacting antibodies from a subject with a protein. Moreover these citations merely contemplate using an immunoglobulin containing fraction from a subject as a detection reagent, rather than a source of immunogenic proteins. Accordingly we submit that all claims are novel over '312.

As for Romain *et al*, this citation merely suggests identification and characterization of a 45/47 kDa antigen complex. Serum from immunized guinea pigs were merely used to screen bacterial cultures filtrates *in vitro* to thereby identify the 45/47 kDa antigen complex. Accordingly, Romain *et al* also requires an *ex-vivo* step of contacting antibodies with a protein. Accordingly we submit that all claims are novel over Romain *et al*.

Similarly, '962, '671 and Ranadive *et al* fail to disclose or suggest isolation or identification of immunogenic proteins endogenously bound to protein complexes comprising an immunoglobulin. In contrast to the presently claimed invitation, the methods described in these citations expressly require an *ex vivo* step of contacting bacterial or cancer-associated antigens

with a biological sample comprising antibodies prior to identifying a protein bound thereto e.g., for determining presence of infection and/or disease or identifying immunogenic antigens. For example, '962 merely suggests screening bacterial cell lysates or cellular protein extracts separated by gel electrophoresis with human serum by Western-blots or Enzyme immunoassays to identify antigens responsible for infection (see Abstract, and Examples 1-3 '962 and e.g., page 3, lines 20-30 '671). Ranadive *et al* merely suggests *in vitro* solid phase radioimmunoprecipitation of bacterial antigens (see page 278, line 1 to page 279, line 18) wherein the antigens are reacted ***in vitro*** with sepharose-conjugated immunoglobulin isolated from serum samples. Accordingly we submit that all claims are novel over '962, '671 and Ranadive *et al*.

Kronberg et al

As for the disclosure by Kronberg *et al*, we submit that amended claim 1 and new claims 204 to 223 are also novel over this document, because Kronberg *et al* do not to disclose or suggest isolation from a subject of any endogenous ***protein complex***, let alone a protein complex comprising an immunogenic ***protein*** or ***protein fragment*** thereof, or identification of any protein antigen or fragment thereof bound to an immunoglobulin the in the protein complex. Specifically, this document at best merely suggests identification of bacterial lipopolysaccharide (LPS) from isolated immune complexes (see e.g., abstract and page 176 column 1). LPS is a major a major bacterial saccharine antigen and not a protein. Accordingly we submit that all claims are novel over Kronberg *et al*.

'766

We also respectfully traverse the allegation that the claims lack novelty over the disclosure in '766 on the basis this citation *inter alia* fails to anticipate identification of an immunogenic protein or fragment thereof bound to the immunoglobulin in the protein complex.

This citation is merely directed to precipitating circulating immune complexes using RhC reagent as indication of a disease or disorder and to separate immune complexes from monomeric immunoglobulins in samples. Notwithstanding that '766 may suggest that immune complexes may be separated into antigen and antibody components by electrophoresis (which is not conceded), the disclosure in '766 goes no further than providing mere invitation to experiment. We respectfully submit that '766 fails to demonstrate identification of any *protein* antigen in the immune complex. None of the Examples in '766 demonstrate that a protein antigen in the circulating immune complexes isolated by the method disclosed in the citation remained intact, let alone demonstrate isolation of any protein antigen from the immune complex or identification of any isolated protein antigen or fragment thereof. As described in the instant application e.g., page 6, lines 3-10, it was conventional wisdom in the art at the priority date of this application that proteins were be rapidly degraded during infection and antigen presentation. In fact, the precise composition of circulating immune complexes was considered at the priority date to be unclear, because general techniques available at that time for detecting immune complexes did not lend themselves to isolation or characterization of antibody or antigen present in the complexes. Accordingly, a person skilled in the art before the priority date of this application would not have construed the disclosure in the '766 patent to mean that any immunogenic protein was actually recovered from an immune complex. In contrast, a skilled artisan would have considered it unlikely at the time that any protein antigen present in the immune complex would remain sufficiently intact to be recoverable from the immunoglobulin.

In contrast to '766, the present application e.g., in Examples 1 and 3 clearly exemplifies isolation and purification of the protein antigens from the immune protein complex and their subsequent identification e.g., by mass spectroscopy and amino acid sequence analysis. In contrast, the methods suggested in '766 merely elute both antigen and immunoglobulin from the RhC complex. The dynamic range between the abundant immunoglobulin in the immune complex and the antigen will make the detection of any antigen in any subsequent electrophoresis extremely difficult.

Based on the unpredictability in the art at the priority date of obtaining from the immunoglobulin fraction of a patient serum intact protein fragments of immunogenic target proteins which are sufficiently large to be identified as being derived from any native protein, let alone to permit their identification of their amino acid sequence, we submit that more than mere invitation to experiment is required to anticipate the claims. Proceeding on this basis, we submit that claim 1 and new claims 204-223 are novel over '766.

In light of the applicant's amendments and submissions, we respectfully request the examiner to withdraw the allegation in respect of claim 1 and new claims 204-223.

Rejections under 35 U.S.C. § 112

In reply to the examiner's allegation that claim 43 is unclear due to certain informalities claim 43 has been cancelled without prejudice or concession, thereby rendering the allegation moot.

Conclusion

Claims 1 and 204-223 are in condition for allowance. A notice of allowance is earnestly solicited. Applicants invite the Examiner to contact the undersigned at 610.640.7855 to clarify any unresolved issues raised by this response.

The Commissioner is hereby authorized to charge any deficiencies of fees and credit of any overpayments to Deposit Account No. 50-0436.

Respectfully submitted,

/Mark DeLuca, Reg. No. 33,229/
Mark DeLuca
Registration No. 33,229

Dated: **September 23, 2010**
PEPPER HAMILTON, LLP
400 Berwyn Park
899 Cassatt Road
Berwyn, PA 19312-1183
Telephone: 610-640-7855
Facsimile: 610-640-7835